Claims

1. A method to prepare a vaccine effective against viral infection which method comprises

providing a mixture of at least one viral protein antigen with a proteosome preparation in the presence of detergent; and

removing detergent from said mixture by diafiltration or ultrafiltration to obtain a proteosome-antigen composition, and

formulating said composition into a vaccine.

2. The method of claim 1 wherein said at least one viral antigen is an antigen derived from influenza virus.

3. The method of claim 2 wherein said at least one influenza antigen is hemagglutinin (HA).

4. The method of claim 1 wherein the ratio of proteosomes to viral antigen in said mixture is greater than 1:1.

5. The method of claim 4 wherein said ratio is at least 4:1.

6. The method of claim 1 which includes more than one viral antigen.

7. A method to prepare a vaccine effective against infection which method comprises

providing a mixture of at least one protein antigen with a proteosome preparation in the presence of a detergent; and

removing detergent from said mixture by diafiltration or ultrafiltration to obtain a proteosome-antigen composition, and

formulating said composition into a vaccine

wherein the ratio of proteosomes to viral antigen in said mixture is greater than 1:1.

8. The method of claim 7 wherein said ratio is at least 4:1.

9. A vaccine prepared by the method of any of claims 1-8.

10. An influenza vaccine which comprises at least one influenza hemagglutinin (HA) formulated with proteosomes in the substantial absence of detergent.

11. The vaccine of claim 10 wherein said HA and proteosomes are in the form of particles with a median size in the range of 150-1,000 nM as measured by light scattering.

12. The vaccine of claim 10 wherein the ratio of proteosomes to influenza HA is greater than 1:1.

13. The vaccine of claim 12 wherein said ratio is at least 4:1.

14. A method to prepare a multivalent vaccine effective against viral infection which method comprises

providing a mixture of at least two viral protein antigens to a proteosome preparation in the presence of detergent; and

removing detergent from said mixture by diafiltration or ultrafiltration to obtain a proteosome-multivalent antigen composition, and

formulating said composition into a vaccine.

15. The method of claim 14 wherein the viral antigens are derived from influenza virus.

16. The method of claim 15 wherein said influenza antigens are hemagglutinin antigens (HA).

17. The method of claim 14 wherein the ratio of proteosomes to viral antigens in said mixture is greater than 1:1.

18. The method of claim 17 wherein said ration is at least 4:1.

19. A method to prepare a multivalent vaccine effective against infection which method comprises

providing a mixture of at least two viral protein antigens to a proteosome preparation in the presence of detergent; and

removing detergent from said mixture by diafiltration or ultrafiltration to obtain a proteosome-multivalent antigen composition, and

formulating said composition into a vaccine wherein the ratio of proteosomes to viral antigens in said mixture is greater than 1:1.

20. The method of claim 19 wherein said ratio is at least 4:1.

21. A method to prepare a vaccine effective against viral infection which method comprises mixing at least two compositions, each containing at least one viral protein antigen, said compositions prepared as described in claim 1 and

formulating said mixture into a vaccine.

22. A method to prepare multivalent vaccine effective against infection which method comprises mixing compositions, each containing at least one protein antigen prepared as described in claim 1 and

formulating said mixture into a vaccine,

wherein the ratio of proteosomes to viral antigens in said mixture is greater than 1:1.

23. A method to elicit an immune response against influenza in a subject which method comprises administering to said subject an amount of the vaccine of claim 10 effective to elicit said response.

24. The method of claim 23 wherein the subject is human.

25. The method of claim 23 wherein said administering is by an intranasal route.

26. The method of claim 25 wherein said administering is by a parenteral route.

27. The method of claim 26 wherein said administering is by an intramuscular injection.

28. An improved method for preparing proteosomes wherein said improvement comprises performing one or more steps comprising precipitation in the presence of ethanol followed by extraction with 0.1-1% detergent solution.

29. An improved method for preparation of proteosomes which method comprises omitting precipitation by ammonium sulfate.

30. The method of claim 1 wherein said detergent comprises more than one detergent.

31. A composition prepared as described in claim 1 which can be filtered with a 0.8 μ filter prior to formulation or filling.

32. A composition prepared as described in claim 7 which can be filtered with a 0.8 μ filter prior to formulation or filling.

33. A composition prepared as described in claim 14 which can be filtered with a 0.8 μ filter prior to formulation or filling.

34. A composition prepared as described in claim 19 which can be filtered with a 0.8 μ filter prior to formulation or filling.